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| 29157 K&L Gates LLP P.O. Box 1135 CHICAGO, IL 60690 | 7590 07/06/2009 | | <div>EXAMINER</div> <div>SWOPE, SHERIDAN</div> | |
| | | | <div>ART UNIT</div> <div>1652</div> | <div>PAPER NUMBER</div> |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

chicago.patents@klgates.com

Office Action Summary

Application No.

10/559,986

Applicant(s)

MCCARTHY ET AL.

Examiner

SHERIDAN SWOPE

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 June 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-44 is/are pending in the application.
- 4a) Of the above claim(s) 5-16 and 22-44 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 and 17-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 03 June 2009 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/083)
Paper No(s)/Mail Date 0609
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Applicants' filing of June 3, 2009, in response to the action of February 3, 2009, is acknowledged. It is acknowledged that Claims 18-21 have been amended. Claims 1-44 are pending. Claims 5-16 and 22-44 were previously withdrawn pursuant to 37 CFR 1.142(b). Claims 1-4 and 17-21 are hereby reexamined.

Drawings- Objections

Objection to Figure 18, for disclosing DNA sequences that are not identified by a sequence identifier number (SEQ ID NO:), is maintained.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Utility

Rejection of Claims 1-4 and 17-21 under 35 U.S.C. 101/112 because the claimed invention lacks patentable utility, for the reasons explained in the prior action, is maintained.

In support of their request that said rejection be withdrawn, Applicants provide the following arguments.

(A) The claimed polynucleotide (SEQ ID NO: 1) has a specific and substantial utility because it encodes a cysteine protease of SEQ ID NO: 2 (CcCP-1) that is expressed in green coffee beans where it may cleave storage proteins in the bean and thus contribute to the bean's flavor and/or aroma profile (specification at paragraphs [0004]-[0008]). Thus, Applicants disclosure provides a well-defined and presently available benefit to the public- modulation of coffee flavor and/or aroma.

(B) The instant specification provides that the polypeptide of SEQ ID NO: 2 has a high level of sequence similarity to several known cysteine proteases (see, e.g., Figure 2). Further, as shown by GenBank protein domain analysis (Exhibit A attached), the polypeptide of SEQ ID NO: 2 comprises a conserved active site. This active site is comprised of a histidine and cysteine diad and is characteristic of a cysteine protease. Thus, sufficient and credible biological evidence exists that the claimed polynucleotide encodes a cysteine protease.

These arguments are not found to be persuasive for the following reasons.

(A) Reply: The specification at paragraphs [0004]-[0008] says nothing about the polynucleotide of SEQ ID NO: 1 or the polypeptide of SEQ ID NO: 2.

(B) Reply: It is acknowledged that Figure 2 provides an alignment of SEQ ID NO: 2 with several other proteins: *Arabidopsis thaliana* (AY070063); *Vicia sativa* (Z99172); *Glycine max* GMCP3 (Z32795); *Glycine max* GmPM33 (AF167986); *Phaseolus vulgaris* Moldavain (Z99955); *Solanum melongena* (AF082181); *Nicotiana tabacum* (AJ242994); *Lycopersicon esculentum* (Z14028); *Vicia faba* (AY161277). However, said alignment is not an assertion that the protein of SEQ ID NO: 2 has the same activity as any one of said proteins. Even if said alignment was an assertion of activity, which it is not, said alignment would not provide evidence that, more likely than not, the protein of SEQ ID NO: 2 has cysteine activity because none of *Arabidopsis thaliana* (AY070063), *Vicia sativa* (Z99172), *Glycine max* GMCP3 (Z32795), *Glycine max* GmPM33 (AF167986), *Phaseolus vulgaris* Moldavain (Z99955), *Solanum melongena* (AF082181), *Nicotiana tabacum* (AJ242994), *Lycopersicon esculentum* (Z14028), and *Vicia faba* (AY161277) has been demonstrated to have a well-established function as a cysteine protease. Moreover, as explained in the prior action, assertion that the

protein of SEQ ID NO: 2 is a cysteine protease is not an assertion of a specific and substantial utility because the family of cysteine proteases is a large and variable family of enzymes with a large number of variable substrates and the potentiality of being involved in many different cellular processes and diseases.

For these reasons and those explained in the prior action, rejection of Claims 1-4 and 17-21 under 35 U.S.C. 101/112 is maintained.

Evidence that a recited protein has a specifically asserted activity can be provided by (i) experimental results demonstrating the recited protein has the asserted activity or (ii) evidence that the recited protein is homologous to a protein that is well-established as having the asserted utility, wherein the recited protein also comprises the domains, motifs, and amino acids required for the asserted activity.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Rejection of Claims 1-4 and 17-21 under 35 U.S.C. 112, first paragraph/enablement, for the reasons explained in the prior action, is maintained.

In support of their request that said rejection be withdrawn, Applicants provide the following arguments. Polynucleotides encoding a polypeptide with at least 70% or 85% homology to SEQ ID NO: 2 are enabled by the instant specification. Procedures and methods for identifying variant polynucleotides that retain the activity of the parental nucleotide are

commonly practiced by a skilled artisan. As shown in Exhibit A (attached), one of skill in the art can readily identify the region of the polynucleotide that encodes for the catalytic active site of SEQ ID NO: 2. Such knowledge allows a skilled artisan to modify a parental nucleic acid without undue experimentation while retaining its catalytic activity, characteristic of a cysteine protease.

These arguments are not found to be persuasive for the following reasons. It is acknowledged that methods for making and testing protein variants for cysteine protease activity were known in the art. However, the specification and Exhibit A fails to provide sufficient guidance such that the making and using of all polynucleotides encoding any protein having at least 70% or 80% identity to SEQ ID NO: 2 is not undue experimentation. The skilled artisan would know that the number of variants increases exponentially as the percent identity goes down. The genus of any protein having 80% homology to a parent protein of 397 residues, as for SEQ ID NO: 2, can be described by $(19_1 + 19_2 + 19_3 + \dots 19_{397})^{20} = 3.5 \times 10^{77}$ variants.

Guo et al, 2004 teaches that the percentage of random single-substitution mutations, which inactivate a protein, using a protein 3-methyladenine DNA glycosylase as a model, is 34% and that this number is consistent with other studies in other proteins (pg 9206, para 4). Guo et al further show that the percentage of active mutants for multiple mutations appears to be exponentially related to this by the simple formula $(.66)^x \times 100\%$ where x is the number of mutations introduced (Table 1). Applying this estimate to the protein recited in the instant application, 80% identity allows up to 80 mutations within the 397 amino acids of SEQ ID NO:2 and, thus, only $(.66)^{80} \times 100\%$ or $3.7 \times 10^{-13}\%$ of random mutants having 80% identity would be active. Similarly, at 70% identity only $2.2 \times 10^{-20}\%$ would be active. Current techniques in the

art (i.e., high throughput mutagenesis and screening techniques) would allow for finding a few active mutants within several hundred thousand or up to about a million inactive mutants, despite even this being an enormous quantity of experimentation that would take a very long time to accomplish. But finding a few mutants within several billion or more, as in the claims to 80% or less identity, would not be possible. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has **not** been provided in the instant specification.

For these reasons and those explained in the prior action, rejection of Claims 1-4 and 17-21 under 35 U.S.C. 112, first paragraph/enablement, is maintained.

Written Description

Rejection of Claims 1-4 and 17-21 under 35 U.S.C. 112, first paragraph/written description, for the reasons explained in the prior action, is maintained.

In support of their request that said rejection be withdrawn, Applicants provide the following arguments. The written description for a claimed genus can be satisfied by disclosure of identifying characteristics, including structural and physical characteristics, functional characteristics coupled with known or disclosed correlation with structural characteristics or a combination of such factors sufficient to demonstrate that the applicant was in possession of the claimed subject matter.

This argument is not found to be persuasive because the specification fails to teach that the polynucleotide of SEQ ID NO: 1, or any variant thereof, encodes a protein having the recited activity. Therefore, the claimed subject matter was not described in the specification in such a

way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

For these reasons and those explained in the prior action, rejection of Claims 1-4 and 17-21 under 35 U.S.C. 112, first paragraph/written description, is maintained.

Allowable Subject Matter

No claims are allowable.

Applicant's amendment necessitated any new grounds of rejection presented in this Office action. Any new references were cited solely to support rejection(s) based on amendment or rebut Applicants' arguments. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Regarding filing an Appeal, Applicants are referred to the Official Gazette Notice published July 12, 2005 describing the Pre-Appeal Brief Review Program.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages. It is also requested that the serial number of the application and date of amendment be referenced on every page of the response.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SHERIDAN SWOPE/
Primary Examiner, Art Unit 1652